Successful Endovascular Salvage of a Pancreatic Graft After a Venous Thrombosis: Case Report and Literature Review

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Abstract
Simultaneous kidney and pancreatic transplant is the criterion standard for treatment of end-stage renal failure because of diabetic nephropathy. Venous thrombosis occurs in approximately 5% of pancreatic transplants, and it is notoriously difficult to treat, forming the most common nonimmunologic cause of graft loss. We report a case of early detection of pancreatic graft venous thrombosis by measuring urinary amylase, resulting in the successful endovascular salvage of the pancreatic graft.

Key words: Pancreas, Transplant, Endovascular

Introduction
Pancreatic transplant offers long-term survival for patients with type 1 diabetes, achieving rates of 85% at 1 year.1 It is particularly valuable when managing end-stage renal failure caused by diabetic nephropathy, combined with a kidney transplant, as there is an increase in patient survival not matched by kidney transplant alone.2,3 However, it is a difficult operation with appreciable morbidity and mortality, and these risks increase significantly after a failed pancreatic transplant.4

Thrombosis of the pancreatic graft’s portal vein is a potentially devastating complication, being notoriously hard to treat and commonly leading to graft failure.1,5,6 Attempts at surgical thrombectomy are often unsuccessful,7,8 and so, medical treatment with systemic anticoagulation is sometimes recommended, especially for partial thrombosis of the pancreatic portal vein.9,10 We describe a case of a pancreatic transplant venous thrombosis that was diagnosed early and successfully and salvaged by using interventional radiologic techniques.

Case Report
The patient was a 46-year-old woman with a 25-year history of type 1 diabetes mellitus. She had end-stage chronic kidney disease because of diabetic nephropathy, for which she had been on peritoneal dialysis and had been experiencing altered hypoglycemic unawareness. Comorbidities included diabetic retinopathy, controlled hypothyroidism, hypertension, hyperlipidemia, and cheiroarthropathy, which affected several joints. She had been smoking cigarettes at the time of transplant assessment, but otherwise had no risk factors for thrombosis, nor any history of thrombotic disorders. A normal dobutamine stress echocardiogram was performed 2 years before the transplant, so a cardiopulmonary exercise test was arranged after transplant assessment. This test demonstrated good cardiac reserve with an anaerobic threshold of 14.9 mL/min/kg and VO2 heart rate response of 8 mL/beat.

Transplant operation
A deceased-donor simultaneous kidney and pancreatic transplant was performed with the pancreas being implanted intraperitoneally in the right iliac fossa, using a donor iliac artery Y graft to the recipient’s right common iliac artery. Venous drainage was by primary Anastomosis from the donor’s portal vein, to the recipient’s common iliac vein, with no venous extension graft. Exocrine drainage was to the bladder. The kidney was
implanted extraperitoneally in the left iliac fossa, with vascular anastomoses to the external iliac artery and vein. The operation was uneventful save for the incidental finding of a right ovarian cyst, for which an attending gynecologist performed a right salpingo-oophorectomy (histology showed this to be a benign endometriotic cyst).

After our normal protocol for pancreatic transplants, 500 mg methylprednisolone was administered intravenously before reperfusion, and 30 mg alemtuzumab was given subcutaneously after reperfusion, with a further dosage of alemtuzumab 2 days later. Maintenance immunosuppression was with tacrolimus and mycophenolate mofetil in a steroid-free regimen.

**Postoperative course**

There was immediate function of both transplants, with euglycemia and no need for exogenous insulin at any time after the transplant. Postoperative capillary blood glucose levels are shown in Figure 1.

![Figure 1. Postoperative Capillary Blood Glucose Levels](image)

The results plotted are for the mean blood glucose level in mmol/L with error bars representing the standard deviation.

Tinzaparin was given at a dosage of 3500 units subcutaneously, once daily, as a prophylaxis for venous thromboembolism. In our center, bladder drainage is routinely used for the exocrine pancreas allowing serial measuring of urinary amylase levels, as a marker of early acute rejection (Figure 2). From the fifth postoperative day, there was a decrease in the urinary amylase concentration, although euglycemia was maintained and so, a contrast-enhanced computed tomography scan was performed on the sixth day to assess the pancreatic graft.

The computed tomography scan demonstrated a venous thrombus extending from the anastomosis at the common iliac vein involving the entire pancreatic transplant portal vein and at least 50% of the length of the pancreatic transplant splenic and superior mesenteric veins. The arterial supply and iliac Y graft were normal. The pancreas transplant itself was enhanced and therefore, was considered to be viable, although there was peripancreatic edema. Based on these findings, an urgent angiography was performed.

**Pancreas transplant angiography and venography**

Access was obtained under ultrasound guidance through the right common femoral artery for the angiogram and the left common femoral vein for the venography. There was normal arterial supply to the pancreas on angiography (Figure 3), but extremely sluggish flow to the veins, with an extensive filling defect (Figure 4). A venous catheter was passed into the pancreatic transplant portal and splenic veins, and the thrombus was laced with 3 mg tissue plasminogen activator. The thrombus then was cleared by a combination of AngioJet and balloon thrombectomy (Figure 5). Completion angiography demonstrated a rapid flow through the transplant and out through the portal vein.

**Postthrombectomy course**

After the thrombectomy, systemic anticoagulation was administered with an intravenous heparin infusion, titrated to maintain activated partial thromboplastin ratio between 1.5 and 2.5, with subsequent conversion to oral warfarin. A Doppler
ultrasound scan was performed 2 days after the thrombectomy, which showed normal arterial and venous flow, with a fully patent pancreatic portal vein, showing normal cardiac variations, which indicated the absence of any significant venous compromise between the pancreatic portal vein and the right atrium.

The patient continued to have excellent function of both grafts throughout her hospital admission, with normal glycemic control, and she was discharged 19 days after the transplant (13 days after the thrombectomy). At no time did she develop hyperglycemia or any further elevation of serum or urinary amylase levels.

**Discussion**

Blood flow in the portal vein in its normal anatomic site varies with the cardiac cycle, but it has a mean volumetric flow rate of 1202.6 mL/min, with Doppler mean flow velocity of 12.3 cm/sec and maximum Doppler mean flow velocity of 31.7 cm/sec. The same vein when draining a pancreatic transplant, alone, has a flow rate of 550 mL/min, resulting in a slow flow velocity. The flow rates also vary within the veins draining from the pancreas, with particularly slow flow in the splenic vein, which receives little drainage from the body and tail of the pancreas itself, and develops areas of stagnant blood at the ligated distal stump where a thrombosis may develop and propagate along the vein.

As a pseudoplastic fluid, the viscosity of blood increases with decreasing flow velocity, and in slow flow states is thus predisposed to thrombosis, a risk that is further increased by the prothrombotic state induced by the systemic inflammatory response to surgery and acute rejection of the graft and by the diabetes mellitus itself. The viscosity of blood and thus, the risk of a thrombosis, is additionally increased by dehydration, which may easily occur in the scenario of difficult fluid management associated with delayed renal graft function and dialysis in a postoperative patient with probable third-space losses.

Management of a pancreatic transplant venous thrombosis is difficult. Surgical exploration with thrombectomy or revision of the anastomosis has a poor success rate, while systemic anticoagulation is likely to be effective when there is partial luminal obstruction from a venous thrombus. In a recent
small series, an endovascular thrombectomy has been reported to be successful after early detection of a thrombosis, but still, it does not appear to be used widely. Overall, the predisposition to a venous thrombosis and difficulty in managing it has been reported as the most common nonimmunologic cause for pancreatic graft loss.

Infarction of a pancreatic transplant has major systemic consequences, making emergency graft pancreatectomy, itself, an operation with significant risk of morbidity and mortality. The clinician and patient are then left with the choice between the technically challenging option of pancreatic retransplant or the potentially unacceptable medium and long-term risk of cardiovascular disease, disablement, and death.

Noting that presenting pancreatic graft venous thrombosis may be easier than a cure, prophylactic anticoagulation has been advocated. They were no thrombosis may be easier than a cure, prophylactic anticoagulation has been advocated. They were no

retransplant or the potentially unacceptable medium and long-term risk of cardiovascular disease, disablement, and death.

We believe that early detection of pancreatic portal vein thrombosis facilitates effective treatment by systemic anticoagulation or radiologic thrombectomy. The traditional markers of hyperglycemia and hyperamylasemia appear to be the late signs of pancreatic dysfunction, and it is notable that all grafts were lost in 1 series when these were used to diagnosthe late signs of pancreatic dysfunction, and it is notable that all grafts were lost in 1 series when these were used to diagnose thrombosis. Although enteric exocrine drainage is now the most commonly used implantation technique, bladder drainage allows for the serial measuring of urinary amylase levels, which have been shown to be an early marker of pancreatic graft injury (eg, acute rejection and reported as a sign of venous thrombosis. The pancreatic graft venous thrombosis in this case was detected by a falling urinary amylase level before any other metabolic derangement occurred, allowing early detection and successful salvage of the graft.

References


